

1. An isolated polynucleotide selected from the group consisting of SEQ ID NO:1, SEQ ID NO:1 wherein T can also be U, and nucleic acid sequences complementary to SEQ ID NO:1.

2. The polynucleotide of claim 1, wherein the polynucleotide is a polydeoxyribonucleotide or a polyribonucleotide.

3. A polynucleotide of claim 1, wherein the polynucleotide is from *Drosophila*.

4. The polynucleotide of claim 1 wherein the polynucleotide is an *Indy* mRNA.

5. A cell comprising the mRNA of claim 4.

6. The cell of claim 5 wherein the cell is a *Xenopus* oocyte.

7. An expression vector comprising a polynucleotide selected from the group consisting of SEQ ID NO:1, SEQ ID NO:1 wherein T can also be U, and nucleic acid sequences complementary to SEQ ID NO:1, wherein the polynucleotide is operably linked to control sequences that direct transcription of the polynucleotide.

8. The expression vector of claim 7 wherein the expression vector is a bacterial or a yeast expression vector.

9. The expression vector of claim 8 comprising pRS426-Gal.

10. The expression vector of claim 7 wherein the expression vector is an amphibian or an insect expression vector.

11. The expression vector of claim 7 wherein the expression vector is a mammalian expression vector.

12. A host cell comprising the expression vector of claim 7.

13. A method of producing an *Indy* polypeptide comprising:

transforming a host cell with an expression vector comprising a polynucleotide selected from the group consisting of SEQ ID NO:1, SEQ ID NO:1 wherein T can also be U, and nucleic acid sequences complementary to SEQ ID NO:1, wherein the polynucleotide is operably linked to control sequences that direct transcription of the polynucleotide;

expressing the polynucleotide in a host cell; and

recovering the *Indy* polypeptide.

14. An isolated polynucleotide encoding an amino acid sequence as set forth in SEQ ID NO:2 or variants of SEQ ID NO:2 comprising conservative amino acid substitutions of SEQ ID NO:2, wherein the variants retain the ability to function as a cellular transporter of carboxylates.

15. The isolated polynucleotide of claim 14, encoding a polypeptide having greater than or equal to 30% overall identity or greater than or equal to 45% overall similarity to SEQ ID NO:2.

16. The isolated polynucleotide of claim 15, wherein the polypeptide is a transporter of carboxylates.

17. The polynucleotide of claim 14, wherein the carboxylate has from two to eight carbons and two or more carboxylic acid groups.

18. The polynucleotide of claim 17, wherein the carboxylate is one or more of succinate, alpha-ketoglutarate, fumarate, or citrate.

19. A polyclonal or monoclonal antibody which binds to a polypeptide of SEQ ID NO:2 or variants of SEQ ID NO:2 comprising conservative amino acid substitutions of SEQ ID NO:2, wherein the variants retain the ability to function as a cellular transporter of carboxylates.

20. The antibody of claim 19 generated by injecting an animal with a polypeptide comprising about 15 to about 30 contiguous amino acids of SEQ ID NO:2.

21. The antibody of claim 20 wherein the polypeptide comprises amino acids 181-197 of SEQ ID NO:2.

22. The antibody of claim 20 wherein the polypeptide comprises amino acids 281-298 of SEQ ID NO:2.

23. A method of isolating an *Indy* gene comprising:
 contacting a genomic library with one or more DNA probes under conditions effective to produce DNA or RNA copies of the *Indy* gene, wherein the DNA probe comprises at least 14 contiguous nucleotides of SEQ ID NO:1;
 producing copies of the *Indy* gene; and
 isolating the copies.

24. The method of claim 23 wherein the *Indy* gene encodes a polypeptide having activity in vivo as a cellular transporter of carboxylates.

25. The method of claim 23 wherein the genomic library is contacted under high stringency hybridization conditions.

26. The method of claim 23 wherein the copies of the *Indy* gene are produced by PCR.

27. The method of claim 23 wherein the genomic library is a mammalian genomic library.

28. The method of claim 23 wherein the library is a human genomic library.

29. An *Indy* gene isolated by the method of claim 23.

30. A method to assess the inhibitory activity of a test substance on a polypeptide having greater than or equal to 25% overall identity or greater than or equal to 30% overall similarity to SEQ ID NO:2, comprising:

contacting the polypeptide with the test substance; and

detecting the amount of carboxylate transported by the polypeptide in the presence and absence of the test substance;

wherein inhibition of transport in the presence as compared to the absence of the test substance indicates that the test substance is a cellular transporter inhibitor.

31. The method of claim 30 wherein the polypeptide comprises SEQ ID NO:2.

32. The method of claim 30 wherein the polypeptide is expressed in a *Xenopus* oocyte comprising an *Indy* mRNA.

33. A method for decreasing the concentration of a polypeptide having greater than or equal to 25% overall identity or greater than or equal to 30% overall similarity to SEQ ID NO:2 in a cell or extract, comprising contacting the cell or extract with a first nucleic acid molecule in an amount effective to inhibit the expression of a second nucleic acid molecule expressing a cellular transporter for carboxylates, wherein the first nucleic acid molecule is substantially complementary to at least a portion of the second nucleic acid molecule.

34. The method of claim 33 wherein the polypeptide comprises SEQ ID NO:2.

35. The method of claim 33 wherein the first nucleic acid molecule is an antisense oligonucleotide, a ribozyme, a triple helix-forming molecule, a double stranded interfering RNA, or a mixture comprising at least one of the foregoing.

36. The method of claim 33 wherein the first nucleic acid molecule further comprises a pharmaceutically acceptable carrier or diluent.
37. A method of calorically restricting an organism, comprising administering to an organism an antagonist of the activity of a cellular transporter of carboxylates in an amount effective to inhibit the activity of the cellular transporter.
38. The method of claims 37, wherein the carboxylates are dicarboxylic acids, tricarboxylic acids, or mixtures thereof.
39. The method of claim 37 wherein the carboxylate is succinate, alpha-ketoglutarate, fumarate, citrate, or a mixture thereof.
40. The method of claim 37 wherein the transporter is a cation-independent transporter.
41. The method of claim 37 wherein the antagonist is at least a portion of an *Indy* gene sequence, an antisense oligonucleotide, a ribozyme, a triple helix-forming molecule, a double stranded interfering RNA, an anti-*Indy* antibody, or a mixture comprising at least one of the foregoing.
42. A substantially pure polypeptide having SEQ ID NO:2.
43. A method of extending lifespan in an organism, comprising administering to an organism an antagonist of the activity of a cellular transporter of carboxylates in an amount effective to inhibit the activity of the cellular transporter.
44. The method of claims 43, wherein the carboxylates are dicarboxylic acids, tricarboxylic acids, or mixtures thereof.
45. The method of claim 44 wherein the carboxylate is succinate, alpha-ketoglutarate, fumarate, citrate, or a mixture thereof.
46. The method of claim 45 wherein the transporter is a cation-independent transporter.
47. The method of claim 43 wherein the antagonist is at least a portion of an *Indy* gene sequence, an antisense oligonucleotide, a ribozyme, a triple helix-forming molecule, a double stranded interfering RNA, an anti-*Indy* antibody, or a mixture comprising at least one of the foregoing

48. A method of treating an organism, comprising administering to an organism a vector comprising SEQ ID NO:1 or an active fragment thereof in an amount effective to increase the body weight of an organism.

49. A transgenic mouse having a genome comprising a disruption in the mNADC-1 gene that prevents expression of functional mNADC-1 protein, wherein the mouse has a phenotype of caloric restriction, weight loss, or life-span extension.

50. A substantially pure polypeptide encoded by a polynucleotide selected from the group consisting of SEQ ID NO:1, SEQ ID NO:1 wherein T can also be U, and nucleic acid sequences complementary to SEQ ID NO:1.

Footnote 6242001